REMARKS

Applicants thank Examiner Steele for the helpful telephonic interview on June 10, 2008 with Applicants' representative, Jacqueline Benn, during which the pending rejections under 35 U.S.C. § 112 and 35 U.S.C. § 103 were discussed.

Information Disclosure Statement

Applicants have submitted a Supplemental Information Disclosure Statement containing copies of references, now labeled C80, C81, C82 and C83, listed on the attached revised form PTO-1449 entitled "List of References Cited by Applicant." Legible copies of references C80, C81, C82 and C83 are submitted herewith. Applicants respectfully request that the references be made of record in the application.

Claims

Upon entry of this amendment, claims 125-126, 128, 131-138 and 141-142 are pending in the present application. Claim 125 has been amended to clarify that Q is a bacterial toxin carrier or another branch identified by its "CJ" reference number, for which support can be found in the instant specification, at, *e.g.*, page 36, lines 15-34. The amendments to claim 125 obviate the rejection under 35 U.S.C. § 112, first and second paragraph. New claims 141 and 142 have been added to include the bacterial toxins described in the instant application. No new matter has been added.

I. Priority

As amended, pending claims 125-126, 128, 131-138 and 141-142 are entitled to priority to U.S. Application No. 08/720,487, filed September 30, 1996, now U.S. Patent No. 5,876,727. Support for linker group CJ 11 is described on page 36, line 9 of U.S. Application No. 08/720,487. Support for the Q group is found on page 36, lines 15-34 of U.S.

Application No. 08/720,487. Support for the bacterial toxin carrier is found in U.S. Application No. 08/720,487 on page 27, line 34 through page 28, line 3, and specifically the bacterial toxins set forth in claim 141 are found on page 28, lines 2-3 of U.S. Application No. 08/720,487.

II. Response to Objections

In response to the Examiner's objection to the format in which the Markush groups were presented in claim 125, the claim as been amended to remove the phrase "selected from the group consisting of." Withdrawal of the objection is respectfully requested.

III. The Claims are not Obvious in Light of Walling and Glenn

Claims 125-126, 128, 131-132 and 136-140 are rejected under 35 U.S.C. § 103(a) as being obvious over Walling et al., U.S. Patent No. 5,164,504 ("Walling") and Glenn et al., U.S. Patent No. 5,980,898 ("Glenn"). Walling teaches cotinine, a nicotine metabolite, as a hapten coupled to a carrier. Walling does not teach nicotine or nicotine derivatives as haptens coupled to a carrier.

In accordance with the teachings of the instant specification, the claimed conjugates which comprise nicotine or nicotine derivatives, which when coupled to a carrier are capable of inducing an antibody response, wherein the antibodies are capable of recognizing the free nicotine molecule, as opposed to metabolites of nicotine (*see, e.g.*, specification at page 105, lines 19-31). In contrast, the antibodies which result from the cotinine-carrier conjugates described by Walling are specific to cotinine. Walling points specifically to the use of cotinine, a natural metabolite of nicotine, due to its much longer half-life than nicotine (*i.e.*, cotinine has a half-life between 7 and 40 hours, while the half-lie of nicotine is less than 30

minutes). Walling also does not teach the use of a bacterial toxin as a carrier. The Examiner attempts to overcome this omission by citing Glenn.

Glenn , however, does not qualify as prior art. Even as acknowledged by the Examiner, the instant claims are entitled to a priority date of September 30, 1996. At best Glenn has an effective filing date of November 14, 1996, and as a result does not qualify as prior art.

Accordingly, reconsideration and withdrawal of the rejection under 35 U.S.C. § 103 in view of Walling and Glenn is respectfully requested.

IV. The Claims are not Obvious in Light of Walling and Glenn in view of Layton

Claims 133-135 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Walling and Glenn in view of Layton et al. Immunity, 59: 459-465 ("Layton"). While Layton describes the use of particular adjuvants, the reference fails to disclose the use of a bacterial toxin as a carrier protein. Further, as discussed in section III, Glenn does not qualify as prior art. Given that Glenn does not qualify as prior art to the pending claims, reconsideration and withdrawal of the rejection under 35 U.S.C. § 103 in view of Walling, Glenn and Layton is respectfully requested.

V. The Claimed Invention Is Not Obvious In View of the Prior Art

The claimed invention relates to hapten carrier conjugates comprising nicotine conjugated to a bacterial toxin. The claimed invention is not obviated by the cited art, in part, because the prior art taken alone or in combination fails to describe or suggest all the claim limitations, for example, nicotine conjugated to a bacterial toxin. *Graham v. John Deere Co.*, 383 U.S. 1, 148 U.S.P.Q. 459 (1966). Thus, the Examiner has failed to establish a case of *prima facie* obviousness. However, assuming *arguendo,* that a *prima facie* case of

obviousness has been made, the Applicants invite the Examiner's attention to the unexpected advantageous and/or superior properties associated with the claimed conjugates. (A *prima facie* case of obviousness is rebuttable by proof that the claimed compounds possess unexpectedly advantageous or superior properties. *In re Chupp*, 816 F.2d 643, 646; 2 USPQ2d 1437, 1439 (Fed Cir 1987)). NicVAX and TA-NIC are two examples of a nicotine-bacterial toxin conjugate formulated as anti-nicotine vaccines and currently in clinical trials for smoking cessation in humans. NicVAX is a nicotine pseudomonas exotoxin conjugate and TA-NIC is a nicotine cholera toxin B conjugate.

The Phase II clinical trials for NicVAX have demonstrated that 6 out of 16 patients who received the vaccine at a dose of 200 μg were able to abstain from smoking cigarettes for at least 30 days during the study, as compared to 2 out of 23 patients that received placebo. (*See,* Hatsukami *et al.*, Clin. Pharmacol. Ther. 200; 76:456-67, IDS Ref. No. C82). In a Phase I, double-blinded clinical study of TA-NIC, 19 of 44 smokers administered TA-NIC had voluntarily given up smoking after six weeks, compared to only 1 of 11 receiving placebo (http://www.medicalnewstoday.com/articles/10723.php, Medical News Today, July 14, 2004, IDS Ref. No. C83).

These clinical trial results indicate that nicotine conjugated to a bacterial toxin can be used efficaciously as a vaccine to treat nicotine addiction. Thus, these clinical trial results support the unexpected advantageous properties associated with the claimed conjugates.

VI. Double Patenting

Claims 125-126, 128 and 131-140 are rejected on the non-statutory ground of obviousness-type double patenting over claims 1-2, 4-5, 8-12 and 17-18 of U.S. Patent No. 5,876,727. Applicants will submit a Terminal Disclaimer under 37 C.F.R. 1.321(c) in connection with the above-identified application.

VII. Provisional Double Patenting

Claims 125-126, 129 and 131-140 are provisionally rejected on the non-statutory ground of obviousness-type double patenting over claims 88-127 of co-pending application 11/472,215. Applicants will submit a Terminal Disclaimer under 37 C.F.R. 1.321(c) in connection with the above-identified application.

Claims 125, 128-129 and 131-140 are provisionally rejected on the non-statutory ground of obviousness-type double patenting over claims 88-118 of co-pending application serial no. 11/472,220. The claims currently pending in application serial no. 11/472,220 relate to a method of using nicotine carrier conjugates for the treatment of nicotine addiction. (*See,* pending claims 119 to 135 in application serial no. 11/472,220; claims 1-118 have been canceled). These claims pending in application serial no. 11/472,220 relate to a separate patentable invention from the composition of matter claims pending in the instant application. This is evidenced by the restriction in the instant application, where claims directed to a method of treating nicotine addiction were deemed to be a separate invention from claims drawn to a hapten-carrier conjugate. (*See,* Office Action, mailed May 1, 2006). Thus, Applicants request reconsideration and withdrawal of the rejection of the claims in view of application serial no. 11/472,220.

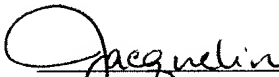
CONCLUSION

Applicants respectfully request that the Examiner consider the amendments and the remarks made herein, and that the Examiner enter them into the record for the present application. Withdrawal of all rejections, and an allowance is earnestly sought. The

Examiner is invited to contact the undersigned attorney if a telephone call could help resolve any remaining items.

Respectfully submitted,

Date: June 12, 2008



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(Reg. No.)

Jacqueline Benn
JONES DAY
222 East 41st Street
New York, NY 10017
(212) 326-3939